REMARKS

Claims 73 and 75-103 were pending in the application upon issuance of the Office Action. Claims 102 and 103 have been withdrawn. Claims 73 and 102 has been amended. No new claims have been added. Applicants reserve the right to rejoin the withdrawn claims. Accordingly, following entry of the foregoing amendment, claims 73 and 75-101 will remain pending in the application.

Support for the amended claim may be found throughout the specification and claims as originally filed. In particular, support for the amendment to claims 73 and 102, can be found at least on page 17, lines 24-28, page 18, lines 19-23, page 20, lines 24-27 and Table-1 of the application as filed. No new matter has been added to the application by way of the foregoing amendment. Accordingly, Applicants respectfully request that the foregoing amendment be entered. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Objection to the Specification

The specification was objected to because there were no Headings in the disclosure. The specification was also objected to on page 1, line 15 in the recitation of "a hormone call FSH" and on page 2, lines 19-20 in the recitation "Assisted Reproductive Technics."

A substitute specification is submitted concurrently herewith to correct the above identified typographical errors and to provide appropriate headings to comply with 37 C.F.R. 1.77(b). Accordingly, reconsideration and withdrawal of the objections is respectfully requested.

Rejection of Claims 83, 84 and 90-94 Under 35 USC § 112, First Paragraph

Claims 83, 84 and 90-94 were rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. The Examiner alleges that the claimed subject matter was not described in the specification in such a way as to convey to one skilled in the art at the time of the invention that the inventor had possession of the claimed invention. (See paragraph 2 on page 5 of the Office Action). The Examiner further asserts that only definitions are disclosed in the specification and no in vivo or in vitro data or examples are disclosed. (See paragraph 3 on page 6 of the Office Action). The Examiner concludes that in the express

absence of one or more examples, evidence and sufficient guidance, a skilled artisan would face undue experimentation for practicing the invention as claimed. (See paragraph 1 on page 7 of the Office Action).

Applicants first respectfully submit that the instant action is unclear with regards to the rejection under 35 USC § 112, first paragraph because the claims stand rejected for lack of written description while the Office Action text references the standard for lack of enablement. It is not clear whether the Examiner intended to reject the claims for lack of written description because the claimed subject matter is not sufficiently disclosed in the specification, or whether he intended to reject the claims for lack of enablement because a skilled artisan would face undue experimentation for practicing the invention as claimed. Appropriate clarification is requested.

Applicant traverses the rejection for failing to comply with the written description requirement. For claims 84-85, written description support may be found throughout the specification as originally filed. In particular, support can be found at least on page 13, lines 1-13 of the application as filed. For claims 90-92, written description support may be found throughout the specification as originally filed. In particular, support can be found at least on page 7, lines 7-14, and page 18, lines 10-14 of the application as filed. For claims 93-94, written description support may be found throughout the specification as originally filed. In particular, support can be found at least on page 7, lines 15-19, and page 18, lines 15-18 of the application as filed.

Furthermore, it was known to one skilled in the art at the time of the invention that cytokines play a role in luteal support. See, for example, page 13, lines 1-13 of the application as filed. It was also known to one skilled in the art at the time of the invention that agents such as SERMs and aromatase inhibitors play a role in stimulating follicular growth. See, for example, page 18, lines 10-14 of the application as filed.

Applicant submits concurrently herewith, a supplemental information disclosure statement. The references in the supplemental information disclosure statement provide further evidence of knowledge to one skilled in the art at the time of the invention that aromatase inhibitors and phosphodiesterase inhibitors play a role in inducing ovulation and/or triggering final follicular maturation.

In addition, the specification provides details on the methods of preparing formulations of the claimed agents and the methods of administering the formulations for treatment. See, for example, page 13, line 15 – page 22, line 33 of the application as filed.

In view of the above, Applicant respectfully submits that one skilled in the art would be enabled without undue experimentation to make and use the invention as claimed. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 73, 75-82, 85-90, 95, 99 and 101 Under 35 USC § 102(b)

Claims 73, 75-82, 85-90, 95, 99 and 101 were rejected under 35 USC § 102(b) as being anticipated by U.S. Patent No. 5,538,948 by Jacobs ("Jacobs"). The Examiner alleges that Jacobs teaches each and every element of independent claim 73. The Examiner asserts that example 1 in Jacobs discloses the protocol of a combined treatment of buserelin/hMG in which GnRH analogue buserelin was injected daily from mid-luteal phase of the previous cycle, the dose of hMG was individually adjusted according to the ovarian response and hCG was administered. The Examiner concludes that Jacobs anticipates independent claim 73 and dependent claims thereon because it meets each and every limitation of the claims as drafted.

As an initial matter, Applicant notes that, solely in the interest of expediting prosecution and in no way acquiescing to the validity of the Examiner's rejection, independent claim 73 has been amended to recite "administering a pharmaceutical agent comprising a gonadotrophin releasing hormone (GnRH) agonist in an amount sufficient to support the luteal phase ..." Support for the amendment may be found throughout the specification. In particular, support for the amendment can be found at least on page 17, lines 24-28, page 18, lines 19-23, page 20, lines 24-27 and Table-1 of the application as filed. No new matter has been added to the application by way of the foregoing amendment.

Accordingly, independent claim 73 as amended requires that the GnRH agonist is administered to the female mammal in an amount sufficient to support the luteal phase *within the first three days after ovulation*. The ovulation can either be spontaneous or triggered by administering at least one additional agent to stimulate follicular growth and to induce final follicular maturation.

Jacobs discloses a combination treatment for infertility in higher mammals including humans. See Abstract. Specifically, Jacobs discloses a treatment for in vitro or in vivo fertilization with gonadotrophins in combination with GnRH analogues and growth hormone.

See column 3, lines 23-37. Jacobs' treatment is directed to dramatically increasing the probability of obtaining fertilized eggs in IVF, i.e. ovulation induction, particularly in women with polycystic ovaries (PCO). See column 2, lines 33-45 and column 3, lines 28-37.

In contrast to the claimed limitation of administering a GnRH agonist within the first three days after ovulation, Jacobs discloses injecting GnRH analogue buserelin daily from mid-luteal phase of the previous cycle followed by treatment with gonadotrophins (hMG) and human chorionic gonadotrophin (hCG) after which oocytes were recovered for in vitro fertilization and the fertilized embryos or unfertilized oocytes were transferred back 2-3 days later. See column 4, lines 20-34.

As depicted in the attached charts (Exhibits A-B), ovulation in humans typically occurs between days 13-15 of the menstrual cycle followed by a luteal phase or secretory phase that typically lasts from day 16 – day 28 of the cycle. According to the claimed method, a GnRH agonist must be administered within the first three days after ovulation i.e. by day 16 where ovulation is at day 13, by day 17 where ovulation is by day 14, and by 18 where ovulation is by day 15. Moreover, according to the claimed method, ovulation can be triggered by an additional agent. This additional agent is administered before and not concurrently/ in combination with a GnRH agonist.

In contrast, Jacobs discloses administering the GnRH analogue from mid-luteal phase of the previous cycle i.e. starting from day 21. Nowhere does Jacobs teach or suggest the claimed timing of administration, namely early luteal phase administration. In fact, Jacobs' goal is to induce ovulation and once the fertilized eggs are recovered, further injections of GnRH are unnecessary. Moreover, Jacobs teaches away from the claimed limitation because according to Jacobs an additional administration of GnRH analogues will desensitize and decrease the number of GnRH receptors which results in very low secretion of FSH and LH which play a role in trigerring ovulation. See column 3, lines 10-15.

In view of the above, Applicant respectfully submits that amended independent claim 73 is patentable over Jacobs at least because Jacobs fails to teach or suggest each and every element of the claim. Claims 75-82, 85-90, 95, 99 and 101 depend directly or indirectly from claim 73 and are therefore also patentable over Jacobs at least for the above mentioned reasons. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 73, 75-82, 85-90, and 95-101 Under 35 USC § 103(a)

Claims 73, 75-82, 85-90, and 95-101 were rejected under 35 USC § 103(a) as being obvious over Jacobs taken with Schmidt-Sarosi et al., J. Assisted Repro. Gen., Vol. 12, No. 3, pages 167-174 ("Schmidt-Sarosi"). The Examiner alleges that Jacobs teaches each and every element of rejected claim except for the administration of buserelin intra-nasally at a dose between 50 and 600 μg or at a dose of 200 μg or at a dose between 50 and 400 μg or at a dose of 100 μg as claimed in claims 96-98 and 100 respectively. The Examiner asserts that Schmidt-Sarosi disclose the intra-nasal administration of a GnRH agonist such as nafarelin which is equivalent to buserelin. The Examiner concludes that it would be obvious to one skilled in the art at the time of the invention to combine the teachings of Schmidt-Sarosi and Jacobs because including intra-nasal administration to Jacobs' methods would obtain the known and recognized functions and advantages thereof. The Examiner further concludes that optimization of dosage for therapeutic use to treat infertility would also be obvious to one skilled in the art at the time of the invention. Applicant respectfully traverses the rejection.

As explained above, Applicant notes that, solely in the interest of expediting prosecution and in no way acquiescing to the validity of the Examiner's rejection, independent claim 73 has been amended to recite "administering a pharmaceutical agent comprising a gonadotrophin releasing hormone (GnRH) agonist in an amount sufficient to support the luteal phase ..." Support for the amendment may be found throughout the specification. In particular, support for the amendment can be found at least on page 17, lines 24-28, page 18, lines 19-23, page 20, lines 24-27 and Table-1 of the application as filed. No new matter has been added to the application by way of the foregoing amendment.

Accordingly, independent claim 73 as amended requires that the GnRH agonist is administered to the female mammal in an amount sufficient to support the luteal phase *within the first three days after ovulation*. The ovulation can either be spontaneous or triggered by administering at least one additional agent to stimulate follicular growth and to induce final follicular maturation.

As explained above, Jacobs fails to teach or suggest each and every element of amended independent claim 73. Schmidt-Sarosi fails to cure this deficiency because Schimdt-Sarosi also fails to disclose administering a GnRH agonist to a female mammal in an amount sufficient to support the luteal phase, within the first three days after ovulation.

Schmidt-Sarosi is directed to comparing the use of human chorionic gonadotrophin (hCG) to that of a GnRH agonist such as nafarelin to support the ovulation inducing effects of

clomiphene. See the paragraphs titled "purpose" and "introduction on pages 167-168. Schmidt-Sarosi discloses that clomiphene citrate was administered on days 5-9 (i.e. during the follicular phase, see Exhibits A-B), and either hCG or nafarelin were administered on cycle day 11 (i.e. during the late follicular phase, see Exhibits A-B). See page 168, column 2, paragraphs 2-4.

Like Jacobs, Schimdt-Sarosi's study discloses methods for ovulation induction to treat infertility. See the "Discussion" paragraph on page 172. Moreover, Schimdt-Sarosi's method results in a low rate of pregnancy establishment and can be labeled as sub-optimal. See column 1, paragraph 1 and column 2, paragraph 2 on page 173.

Applicant respectfully submits that Jacobs or Schmidt-Sarosi, either alone or in combination, fail to teach or suggest at least administering a GnRH agonist to a female mammal in an amount sufficient to support the luteal phase *within the first three days after ovulation.* Moreover, a skilled artisan at the time of the invention would be motivated not to combine the methods of Jacobs and Schmidt-Sarosi because the results obtained by Schmidt-Sarosi for treatment of infertility by intra-nasally administering a GnRH agonist such as nafarelin, are sub-optimal and result in a low rate of pregnancy as illustrated by drastically suppressed LH levels and lower E2 and progesterone levels on day LD 13 compared to the hCG control. See column 1, paragraph 1 on page 171 and Figures 3-4.

In view of the above, Applicant respectfully submits that amended independent claim 73 is patentable over Jacobs taken with Schmidt-Sarosi. Claims 75-82, 85-90, and 95-101 depend directly or indirectly from claim 73 and are therefore also patentable over Jacobs taken with Schmidt-Sarosi at least for the above mentioned reasons. Reconsideration and withdrawal of the rejection is respectfully requested.

If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 227-7400.

Please charge our Deposit Account No. 12-0080 to cover the extension of time fee. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 12-0080, under Order No. KZY-001US.

Dated: July 21, 2009

Respectfully submitted,

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Exhibit A

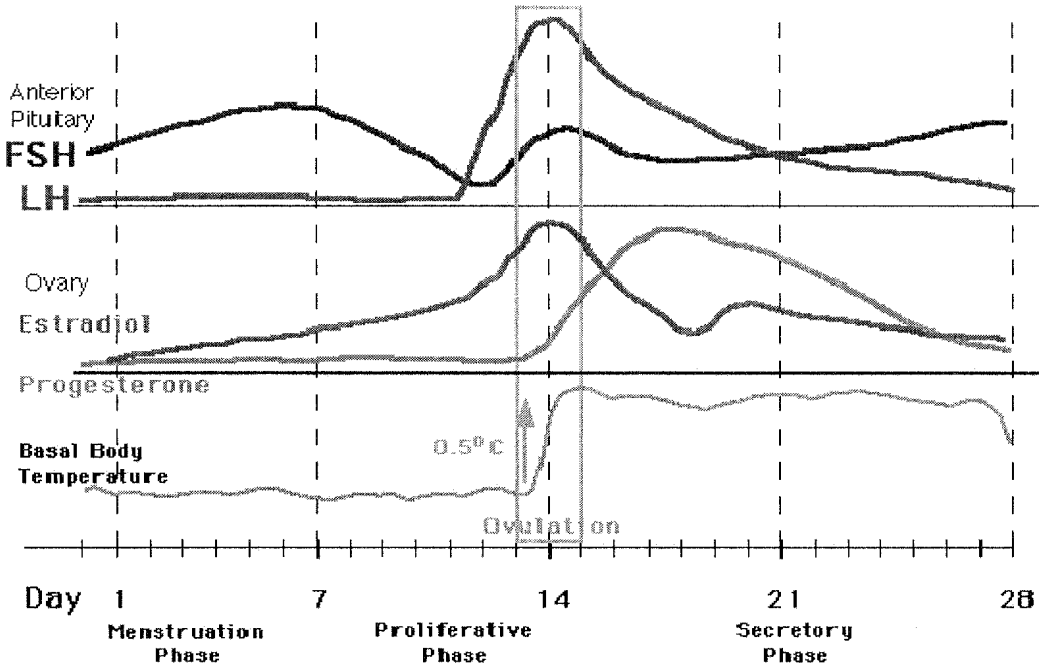
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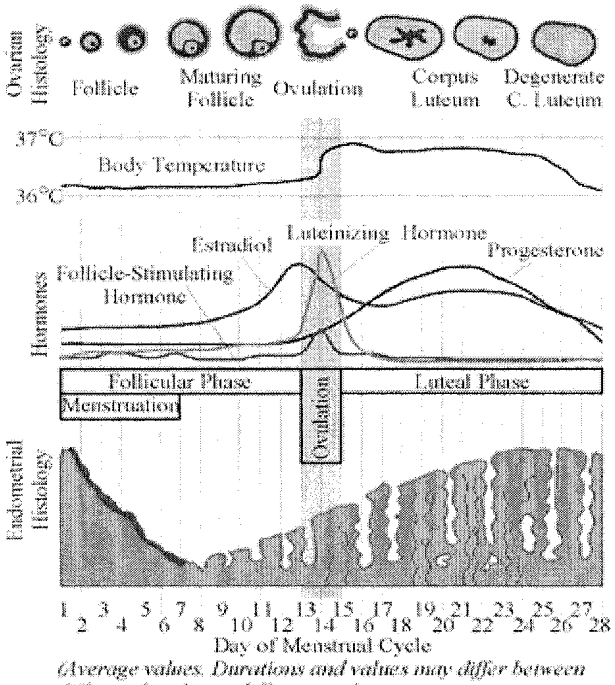
Exhibit B



(Average values. Durations and values may differ between different females or different cycles.)